

REMARKS

This paper is submitted in response to the Office Action mailed April 3, 2007 for the above-identified patent application. Claims 1-7, 10, 12-14, and 19 have been rejected. Claims 3-4, 8-10, 15-18, and 20-21 have been canceled. Claim 11 has been withdrawn from consideration. Claims 1, 2, 5, 6, and 7 have been amended. No new matter has been added. Claims 1, 2, 5-7, 12-14, and 19 are now pending.

I. The Rejections under 35 U.S.C. 112, second paragraph

The Examiner has rejected claims 1-3, 7, 10, and 12-13 under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement. Applicants have amended independent claim 1 to recite the compounds explicitly named at pages 10-13 of the specification (*i.e.*, milnacipran, bicifadine, sibutramine, venlafaxine, and duloxetine). Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

II. Rejections under 35 U.S.C. § 103

Claims 1-7, 10, 12-14 and 19 have been rejected under 35 U.S.C. 103(a) as obvious over U.S. Patent No. 4,478,836 to Mouzin *et al.* ("Mouzin") and Moret *et al.*, NEUROPHARMACOLOGY, 24:12, 1211-19 (1985) ("Moret") in view of Ruoff, J. FAMILY PRACTICE, 43:6, S25-S34 (1996) ("Ruoff").

The Examiner states that Mouzin and Moret disclose that milnacipran is a dual norepinephrine serotonin reuptake inhibitor (NSRI) that may be used to treat depression. Ruoff discloses that "once depression is diagnosed, treatment in the patient with chronic pain is no different than in patients without pain." Thus, the Examiner alleges that it would have been obvious for a person skilled in the art to use the claimed compounds to treat of depression secondary to pain.

Applicants respectfully disagree. Depression secondary to pain is a disorder characterized by co-morbidity of pain and *atypical* depression. In contrast, Mouzin, Moret and Ruoff disclose the treatment of depression - not atypical depression. Atypical

depression is a distinct subtype of depression that is defined as “a type of depression that responds preferentially to monoamine oxidase inhibitors (MAOIs).” Davidson, J. CLIN. PSYCHIATRY, 68 Suppl 3:10-5 (2007) (attached). Although some patients with chronic pain express characteristics of atypical depression, depression with pain is different than atypical depression. *See* Specification paragraphs 4-6.

Ruoff discloses that SSRIs are the *first-line treatment* for depression because of the demonstrated efficacy, and well-tolerated side-effect profile, in comparison to MAOIs. *See* Ruoff page S28. Ruoff is clearly not concerned with atypical depression since it discloses that MAOIs - the preferred treatment for atypical depression - should be used as third-line treatment for depression. *See* Ruoff page S32. Thus, one skilled in the art would understand that, at most, Ruoff discloses that the treatment of *depression* is no different in patients with or without pain.

Furthermore, Ruoff does not teach or suggest the treatment of atypical depression with an NSRI. Rather, the disclosure of Ruoff would lead a person of ordinary skill in the art away from using an NSRI to treat atypical depression as presently claimed. Ruoff discloses that therapy with an NSRI, such as venlafaxine, is associated with serious side effects including nausea, vomiting, blood pressure increase, sexual dysfunction, sweating and somnolence. *See* Ruoff page S30. In fact, Ruoff discloses that, due to its side effect profile, the NSRI venlafaxine should be reserved for use in the treatment of refractory depression. *See* Ruoff page S30. Thus, Ruoff not only fails to teach the desirability of the claimed method, but teaches away from using an NSRI. Consequently, Ruoff, alone or in combination with Mouzin or Moret, does not teach or suggest the treatment of *atypical* depression secondary to pain as presently claimed. Thus, reconsideration and withdrawal of the rejection of claims 1-7, 10, 12-14 and 19, as obvious under 35 U.S.C. 103(a) is respectfully requested.

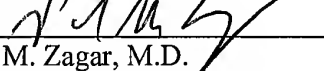
III. Conclusion

In view of the foregoing remarks, reconsideration and allowance of claims 1, 2, 5-7, 12-14, and 19 is respectfully requested.

Applicants believe that the claims are now in a condition for allowance. However, if the Examiner believes that any outstanding issues could be resolved by an interview, the Examiner is asked to contact the undersigned below.

Dated: August 2, 2007

Respectfully submitted,

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